tunately tests for this operation are done at the expense of considerable material, as it is necessary to use a large quantity for each count.

The above impressions are merely a very brief summary of the work now being carried out in Sweden on the material collected by the Swedish Deep-Sea Expedition, and in no way has space allowed for a complete survey. Let it be said that Prof. Pettersson has succeeded in building up a great network of scientific research on his cores both in Sweden, in north-west Europe, in Great Britain and in the United States. Every core, whether isolated or one of a group or sequence, is of value from some aspect of the deep-sea floor, which is so little known. It is not possible at this early stage to assess the worth of the work, whether geophysical, geochemical, biological or palæoclimatological. It is, however, evident even at this early stage that, whatever the aspect of approach, the whole will gradually be dovetailed into a preliminary story which will be a guide to future workers and explorers in this field in the same manner that the great *Challenger* Expedition of the last century became the foundation of oceanographical work to the present generation of marine investigators. We must therefore look forward with hope to co-ordinating this work further in August at the meeting of the Association d'Océanographie Physique in Brussels. It is essential to encourage co-operation in all the varied lines of study of the cores, because, however great the difficulties in obtaining sufficient financial assistance for this all-important work, collaboration, and not rivalry, is of prime importance; without it, what little money that is at present available would largely be wasted.

AN EXTRA-ADRENAL ACTION OF ADRENOTROPIC HORMONE

By Prof. HANS SELYE

Institute of Experimental Medicine and Surgery, University of Montreal

JUST fifteen years ago, I described in this journal the 'general-adaptation-syndrome' as the somatic expression of "the response to damage as such". It was surprising that all organs of the body show degenerative changes, with widespread pyknosis and catabolism, under the influence of various damaging agents; only the adrenal cortex exhibits signs of increased hormone secretion and cellular proliferation. This was ascribed to the increased production of 'adrenotropic hormone', now generally known as ACTH[1]. These observations lead us to the concept that non-specific damage, or 'stress', has its own physiology and pathology (quite apart from specific actions of the agent used to produce stress) and that the pituitary-adrenal system plays a cardinal part in this non-specific adaptive or defensive reaction[2,3].

Subsequent investigations showed that the acute thymus involution, which occurs during the first 'alarm-reaction' stage of the general-adaptation-syndrome, is prevented by suprarenalectomy, while active adrenocortical extracts can produce thymus involution, even in the adrenalectomized animal. Hence, I concluded that "the secretion of the adrenal gland must therefore be considered essential for the ability of the thymus to undergo sudden involution"[4]. Since after hypophysectomy stress causes neither adrenocortical stimulation nor thymus involution, it was thought that the thymolysis is elicited by stress through the discharge of adrenotropic hormone and the consequent increase in the production of corticoids[2].

The numerous pertinent reports, published during the intervening years, appeared to support this concept; indeed, it is now generally held that not only the thymolytic, but also all known actions of adrenotropic hormone are mediated through the hormones of the adrenal cortex, because adrenotropic hormone produces no obvious changes in adrenalectomized animals, or in patients with complete adrenal destruction[5].

Recent experiments revealed that many of the actions of somatotrophic hormone are likewise abolished by adrenalectomy and can be restored, even in adrenalectomized animals, by suitable treatment with corticoids (Selye, in the press). This raised the question whether some of the supposedly trans-adrenal actions of adrenotropic hormone might not also be direct, though dependent upon the simultaneous presence of corticoids in the body fluids. The results to be reported here show that such a peripheral synergism between adrenotropic hormone and corticoids does, in fact, exist. Concurrent treatment with adrenotropic hormone and cortisone caused pronounced thymolysis in the adrenalectomized rat, although each of these hormones given separately failed to do so at the same dose level.

Experimental procedure. Three experiments have been performed on a total of 120 female piebald rats. In each of these we used four groups of ten rats treated respectively as follows: (I) hypertensinogen: (II) adrenotropic hormone; (III) adrenotropic hormone and cortisone; (IV) hypertensinogen and cortisone. Hypertensinogen was administered merely in order to determine the possible effect of a non-hormonal foreign protein. It was given at a daily dose-level of 6 mgm., administered in the form of six subcutaneous injections of 1·0 mgm. in 0·1 ml. of saline, subcutaneously every four hours. Adrenotropic hormone (ACTH, Connaught Laboratories, Toronto, Lot No. 2–2, 3–1) was given at the same dose-level and in the same manner as the hypertensinogen. It will be recalled that in order to obtain maximal adrenocorticotrophic effects from adrenotropic hormone, it is essential to give it at short intervals; it is for this reason that injections were given every four hours during the day and night. Cortisone was administered in the form of one subcutaneous injection of 0·5 mgm. a day, in the form of a microcrystalline suspension (as distributed by Merck and Co., Ltd., Montreal) which contains 5 mgm. of cortisone acetate per ml.

All the experimental animals in the three series were bilaterally adrenalectomized and ovariectomized forty-eight hours before the initiation of the injections. Immediately after this, they were given 1 per cent sodium chloride instead of tap water as a drinking fluid. The removal of the gonads and adrenals was necessary in order to eliminate both the known endogenous sources of steroid hormones.

The three experimental series differed only in that injections were given in the first experiment during four days, in the second during six days, and in the third during nine days. At the end of each experiment the animals were killed by exsanguination and their thymus glands removed for weighing and histological study.

Table 1. Effect of Four Days Treatment

Treatment		Hypertensinogen	ACTH	ACTH + cortisone	Hypertensinogen + cortisone
Body-weight (gm.)	Initial	121	121	121	121
	Final	117	109	114	120
Weight of thymus	in mgm.	366	319	203	282
	in mgm./100 gm. body-weight	308±18·5	294±16·1	179±15·9	237±18·1

Table 2. Effect of Six Days Treatment

Treatment		Hypertensinogen	ACTH	ACTH + cortisone	Hypertensinogen + cortisone
Body-weight (gm.)	Initial	108	108	108	107
	Final	109	104	104	109
Weight of thymus	in mgm.	299	291	161	249
	in mgm./100 gm. body-weight	275±23·5	280±21·8	156±13·7	228±17·4

Table 3. Effect of Nine Days Treatment

Treatment		Hypertensinogen	ACTH	ACTH + cortisone	Hypertensinogen + cortisone
Body-weight (gm.)	Initial	110	110	110	109
	Final	129	108	118	131
Weight of thymus	in mgm.	423	303	168	283
	in mgm./100 gm. body-weight	324±18·1	280±15·6	141±16·4	217±12·6

Results. The details of the experimental arrangement, the initial and final body-weights, as well as the thymus weight expressed in mgm. and in mgm. per 100 gm. of body-weight (the latter with its standard error) are given in the accompanying tables.

It will be noted that none of the injected materials caused a significant loss of body-weight during our short-term experiments. Neither adrenotropic hormone nor an equivalent amount of non-hormonal protein (in the form of hypertensinogen) produced any consistent and significant involution of the thymus in these adrenalectomized rats. Cortisone, when given in conjunction with hypertensinogen, induced only a moderate degree of thymolysis. However, in all three series, marked involution of the thymus was noted in the animals given adrenotropic hormone and cortisone. Statistical analysis of the apparent differences between groups III and IV showed that in all three series the augmentation of cortisone thymolysis by adrenotropic hormone was significant. The value of P, in comparing the thymus weights in mgm. per 100 gm. between groups III and IV, was $< 0{\cdot}05$ in group I, and $< 0{\cdot}01$ in groups II and III.

Histological studies essentially confirmed the observations made by mere weighing of the thymus in that maximal thymolytic phenomena were noted in groups III of all three series.

Discussion. These data indicate that adrenotropic hormone can synergize the thymolytic effect of a corticoid hormone, such as cortisone, even in the absence of the adrenal cortex. It follows that the thymolytic effect of stressor agents is not necessarily due to increased production of corticoids through discharge of adrenotropic hormone, but that it may in part also result from a peripheral synergism between the hormone and the corticoids.

These findings call to mind certain observations made in this Institute by Dr. Herlant[6], who showed that the thymolytic effect of threshold doses of adrenocortical extract is increased by an alarm-reaction, even in adrenalectomized rats. The present observations suggest that this increase may have been due, at least in part, to an endogenous discharge of adrenotropic hormone by the pituitary of the animal exposed to stress.

It remains to be seen whether a disproportion between circulating adrenotropic hormone and corticoids can produce results qualitatively different from those normally elicited by either of these hormones, and whether conjoint treatment with the hormone and cortisone would be of special benefit in the treatment of those lymphatic, inflammatory and allergic diseases which respond favourably to glucocorticoids.

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ANTITUBERCULOUS EFFECT OF CERTAIN SURFACE-ACTIVE POLYOXYETHYLENE ETHERS IN MICE

By Dr. J. W. CORNFORTH, Dr. P. D'ARCY HART, R. J. W. REES and J. A. STOCK

National Institute for Medical Research, Mill Hill, London, N.W.7

As part of a study, by two of us (P. D'A. H. and R. J. W. R.), of factors influencing the susceptibility of mice to experimental tuberculosis, methods of altering the body lipids were sought. For this purpose a new technique[1–3], by which the blood cholesterol and phospholipids could be maintained at high levels for several weeks by the repeated intravenous injection of the non-ionic surface-active agent 'Triton *A*20', was tried. This agent is described by its manufacturers (Rohm and Haas Co., Philadelphia; we are indebted to their associates, Charles Lennig and Co., Ltd., London, for supplies of the substance) as a 25 per cent aqueous solution of an arylalkyl polyether of phenol ('Triton *WR*1339'); and all doses of Triton *A*20 given below refer to this anhydrous material. In the first experiment, made more than a year ago, 'Triton *A*20' produced a striking suppressive effect on the course of a moderately acute tuberculous infection in mice. Further experiments amply confirmed this unexpected observation. 'Triton *A*20' has, however, undesirable toxic effects in mice. Injection of the optimal intravenous chemotherapeutic doses (15–25 mgm.) is followed immediately by convulsions, though these are transitory and seem to leave no after-effects; while